

098766-13

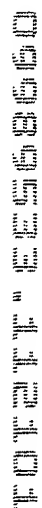


FIG. 2

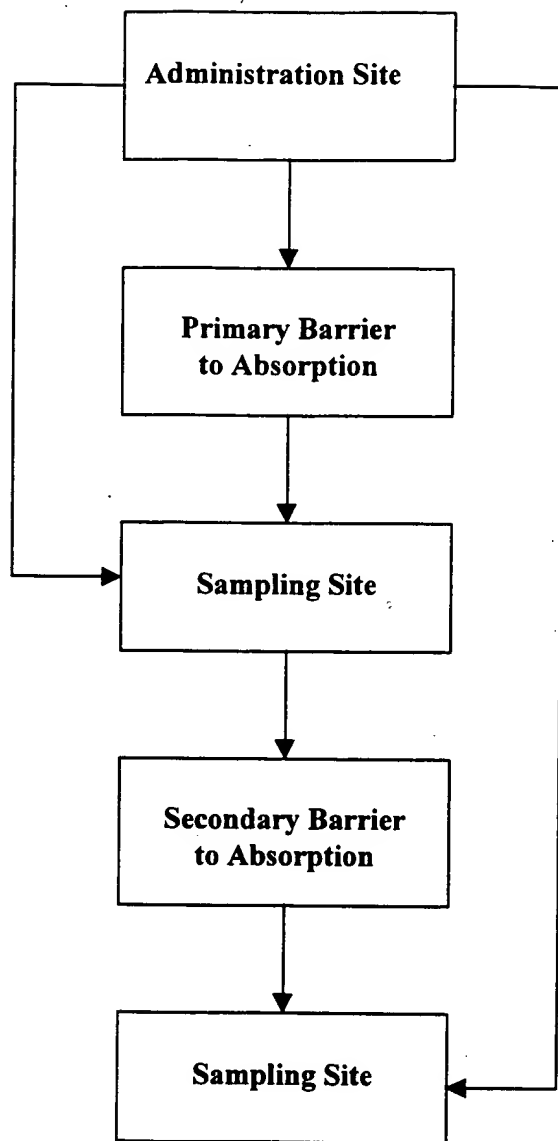


FIG. 2

FIG. 3

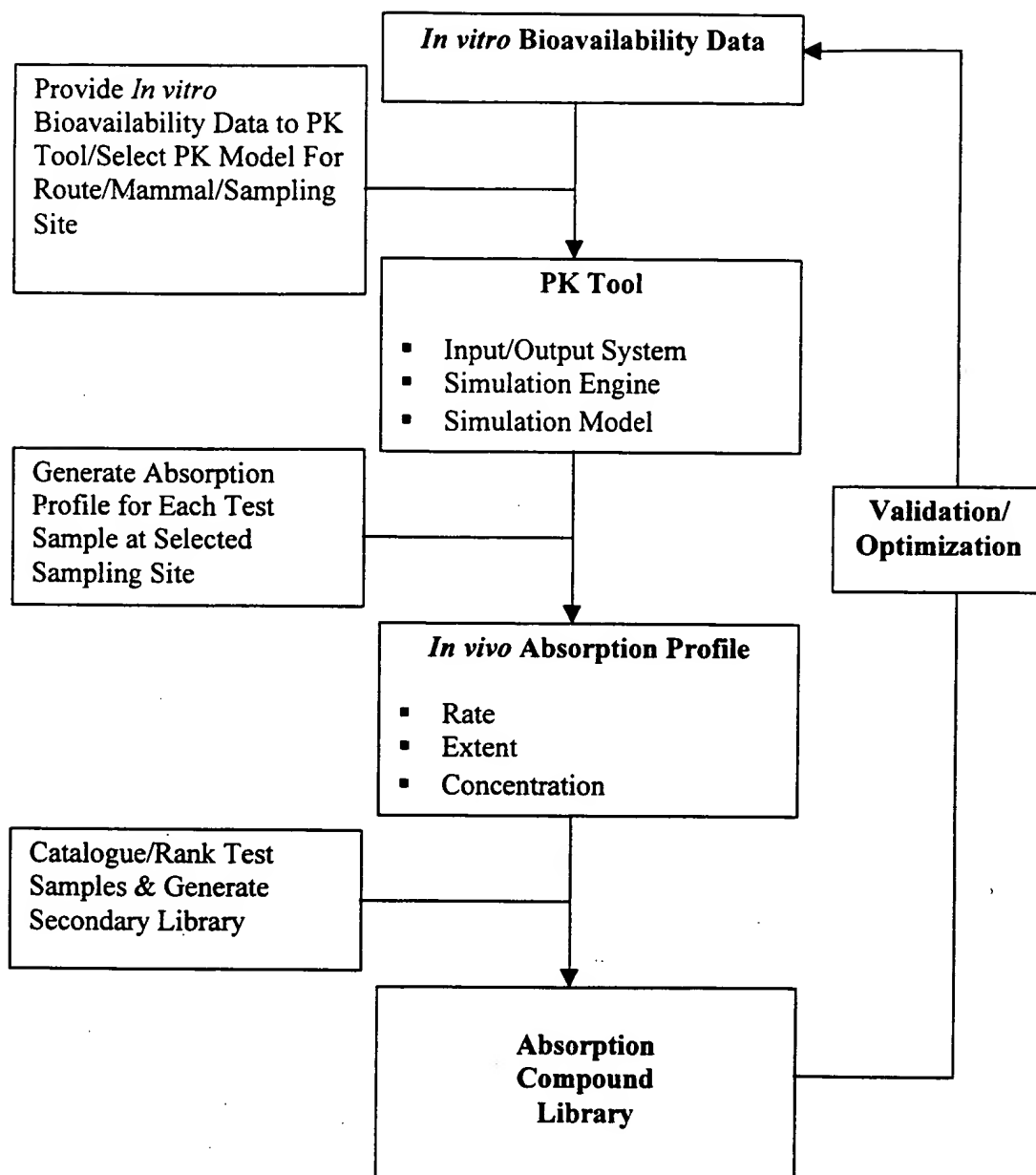


FIG. 3

FIG. 4

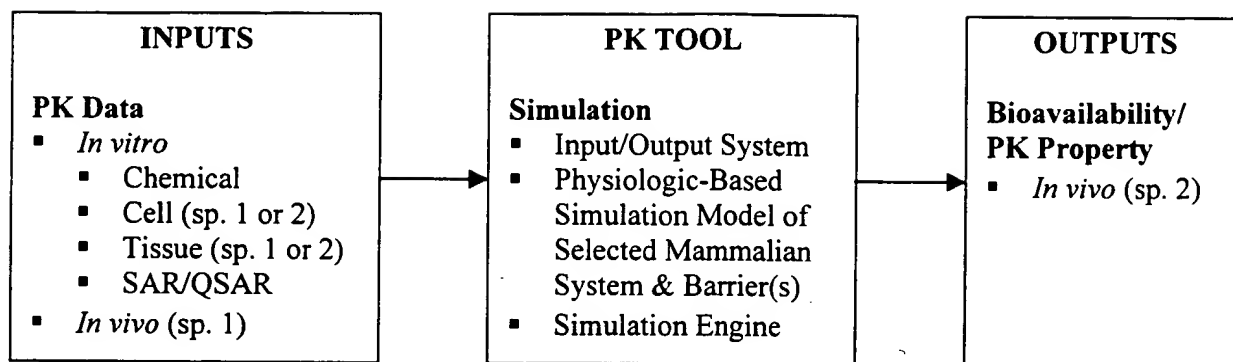


FIG. 5

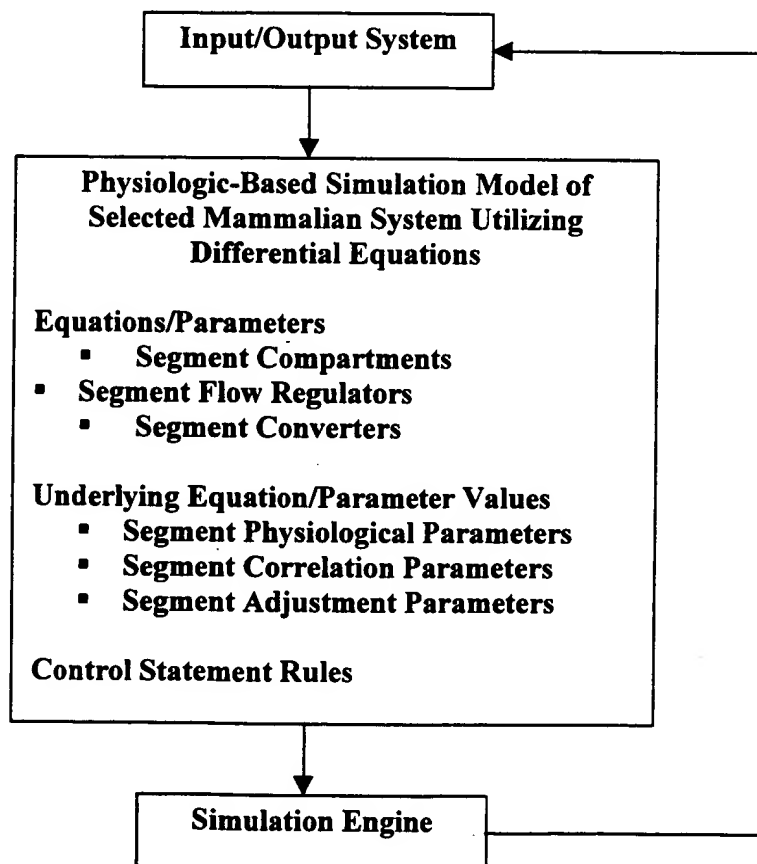


FIG. 4

FIG. 6

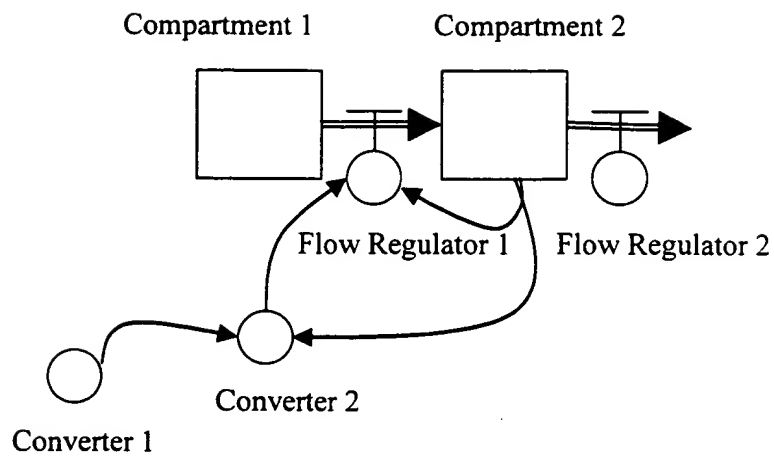

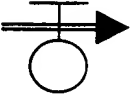




FIG. 7

Symbol	Name	Time-Dependent Function
	Compartment	Equation or value for amount of substance stored.
	Flow Regulator	Rate equation for amount of substance transferred.
	Converter	Equation or pre-defined value for (i) input into flow regulator; (ii) input into another converter; and/or (iii) storing value.
	Input Link	Directs input values.

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FIG. 8

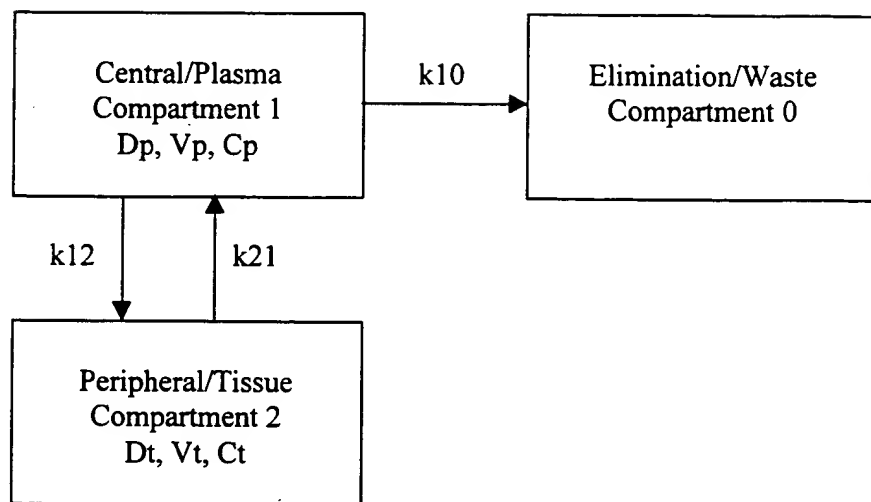


FIG. 9

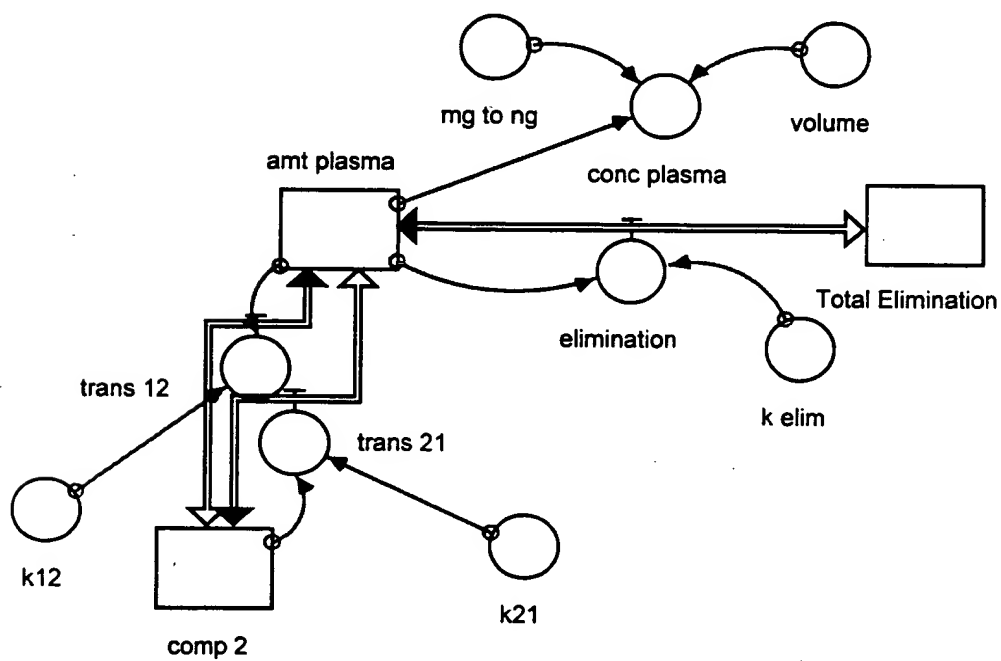


FIG. 10

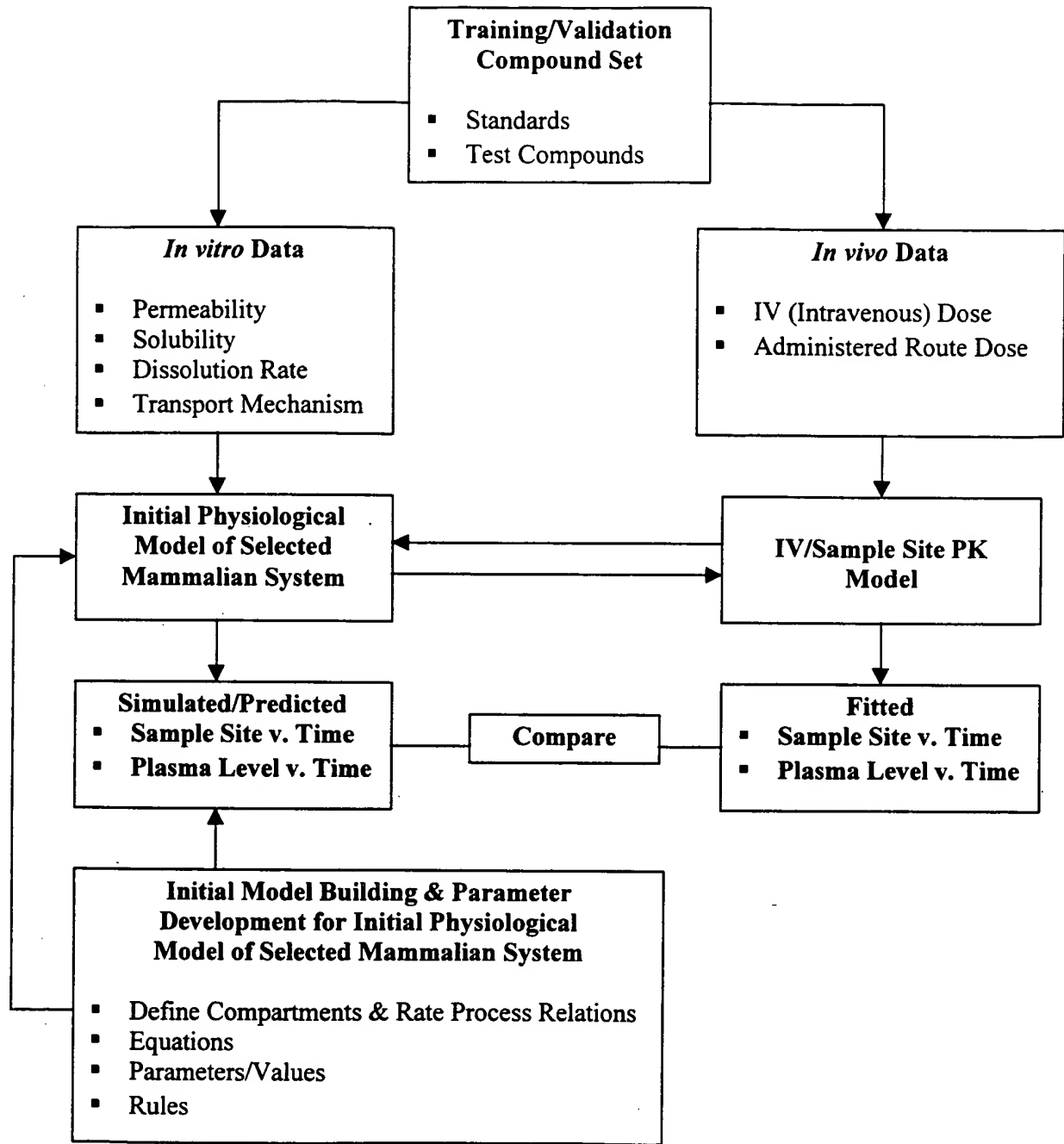


FIG. 10

FIG. 11

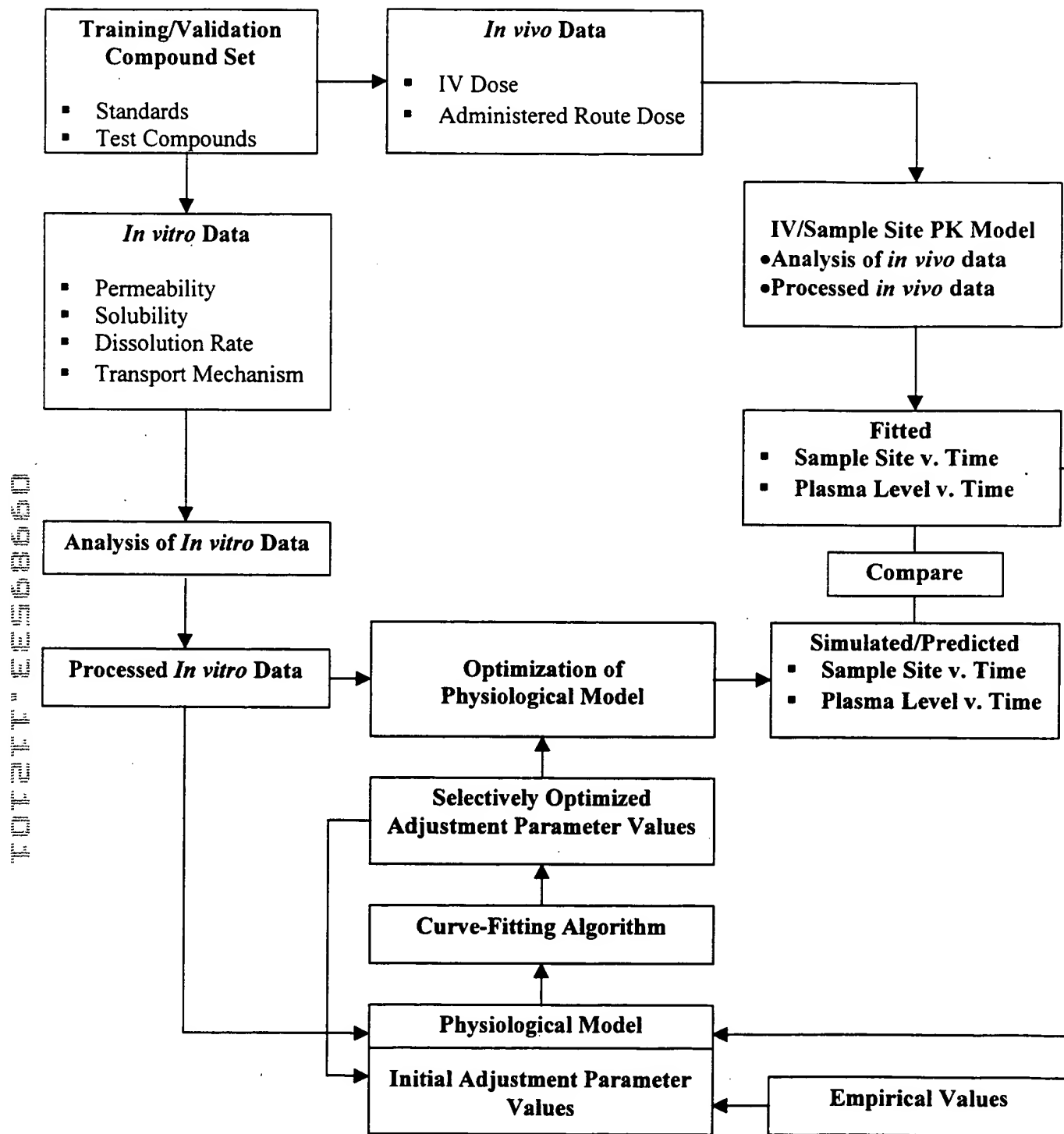


FIG. 12

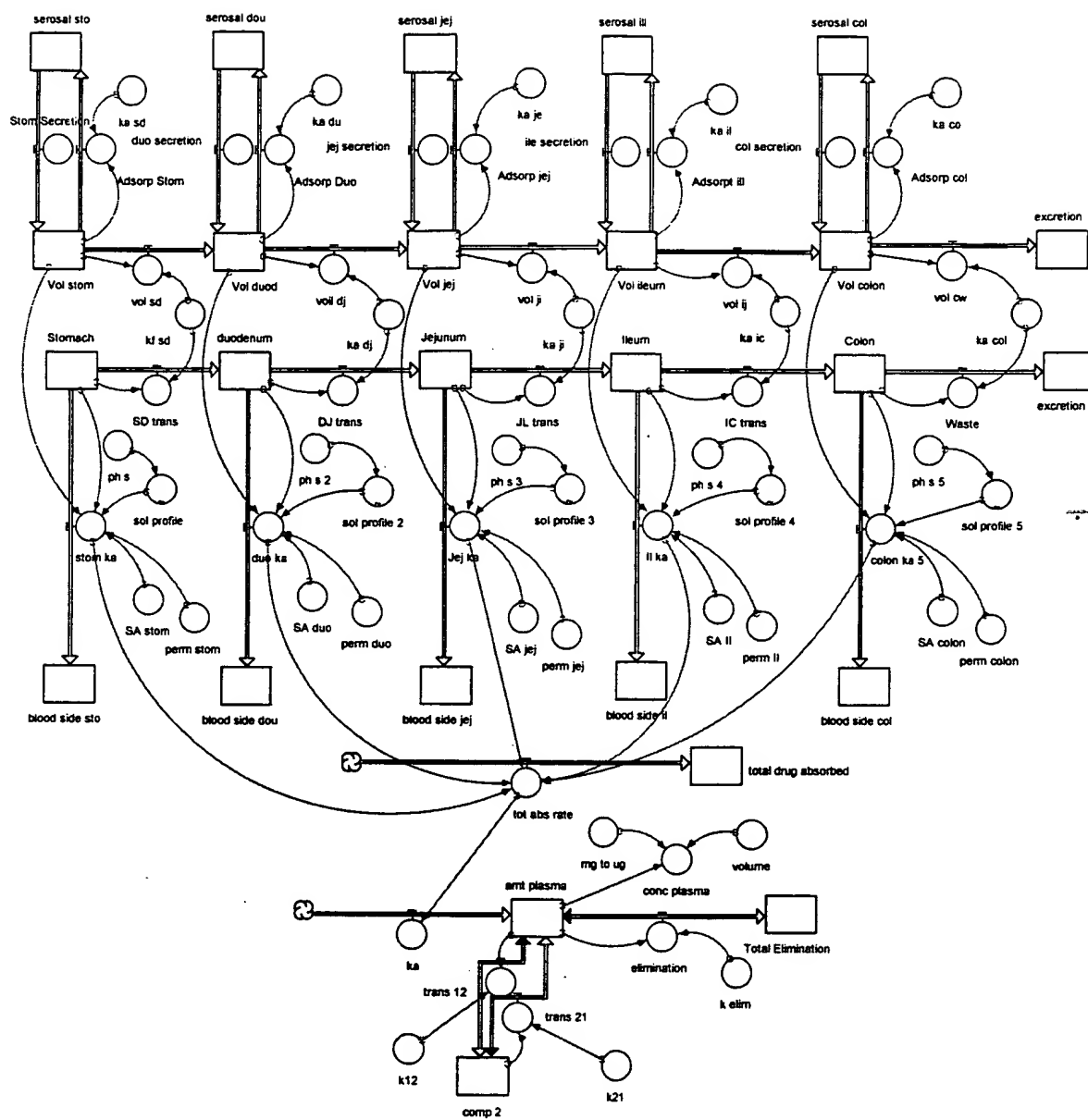


FIG. 13

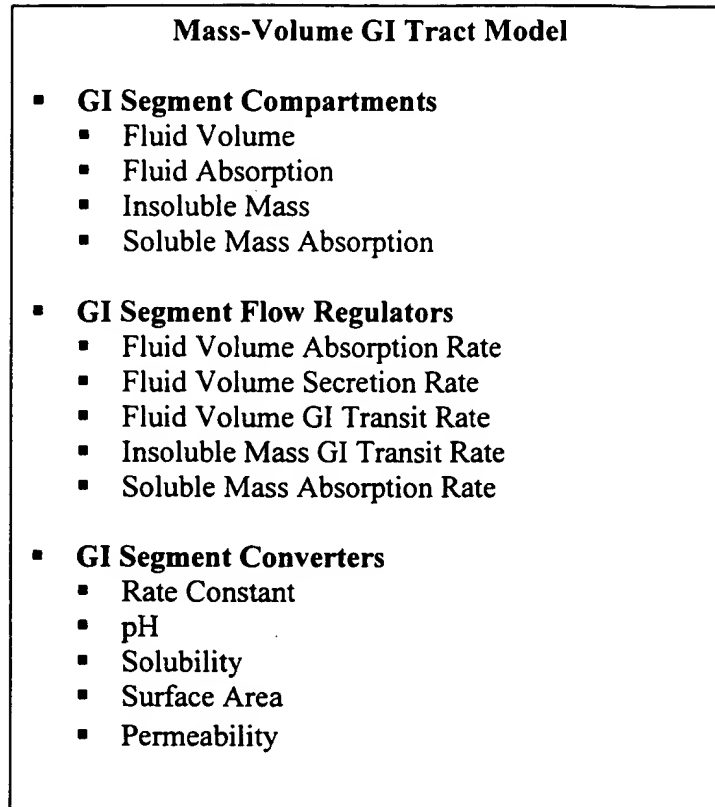


FIG. 14

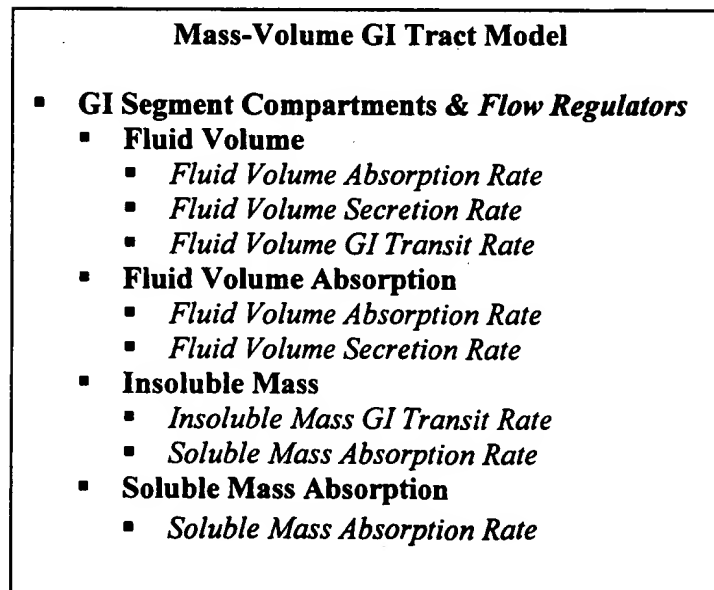


FIG. 15

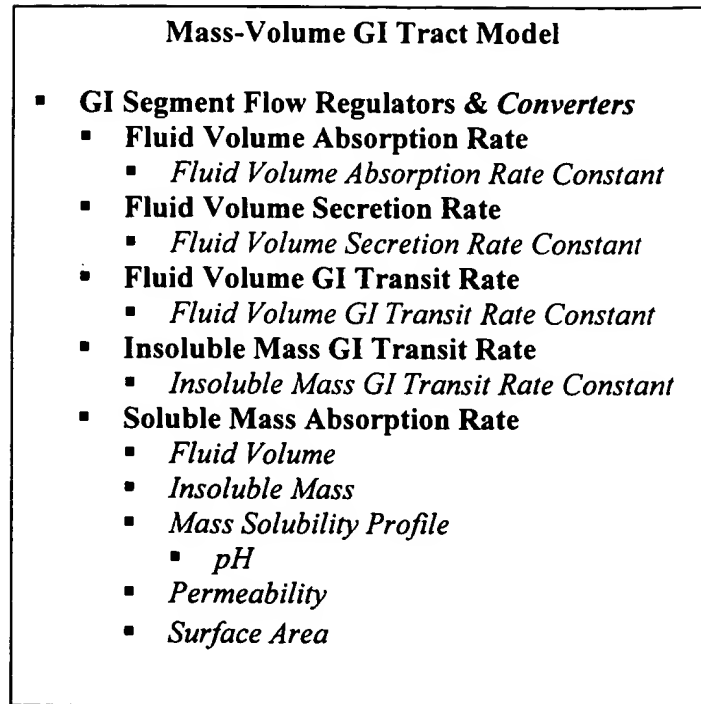


FIG. 16

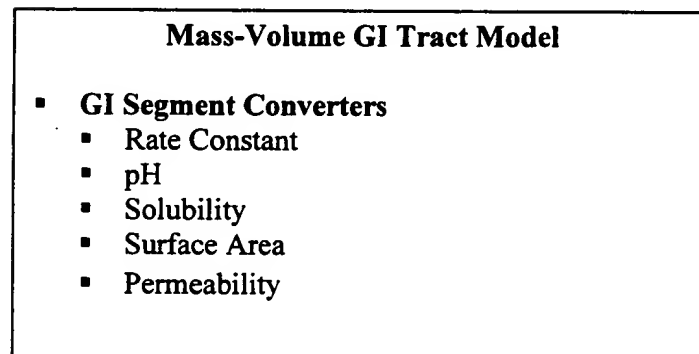


FIG. 17

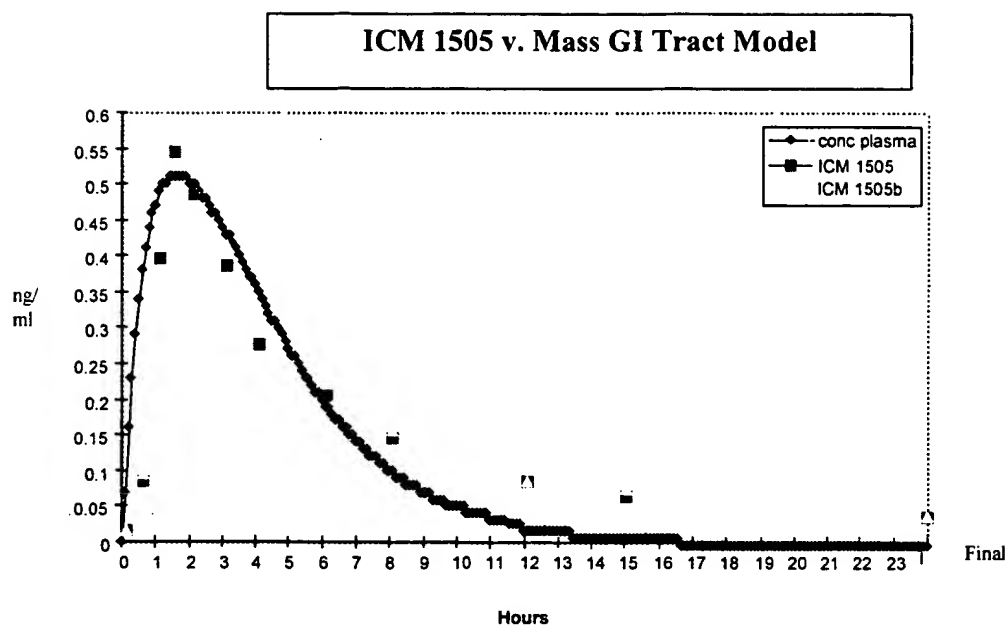


FIG. 18

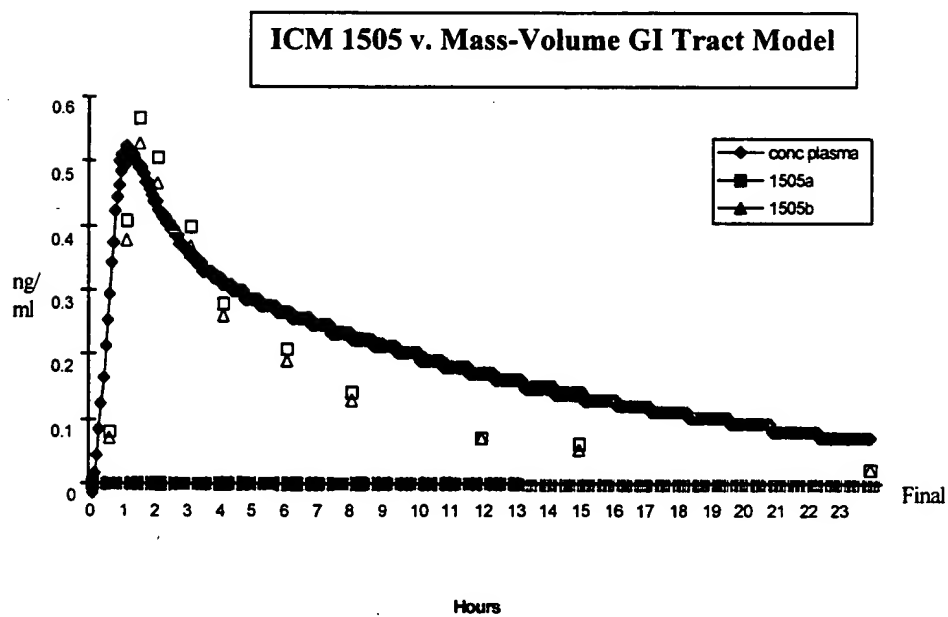


FIG. 19

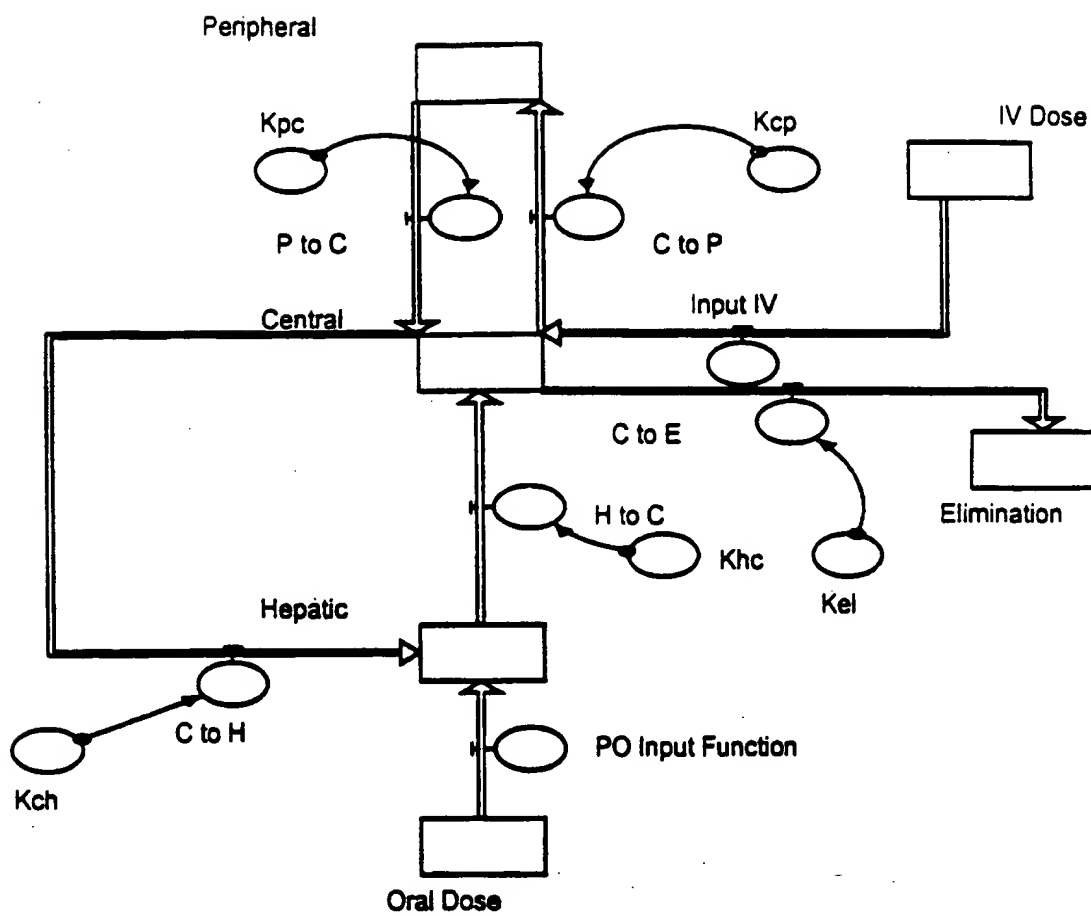


FIG. 19 "CE568660"

FIG. 20

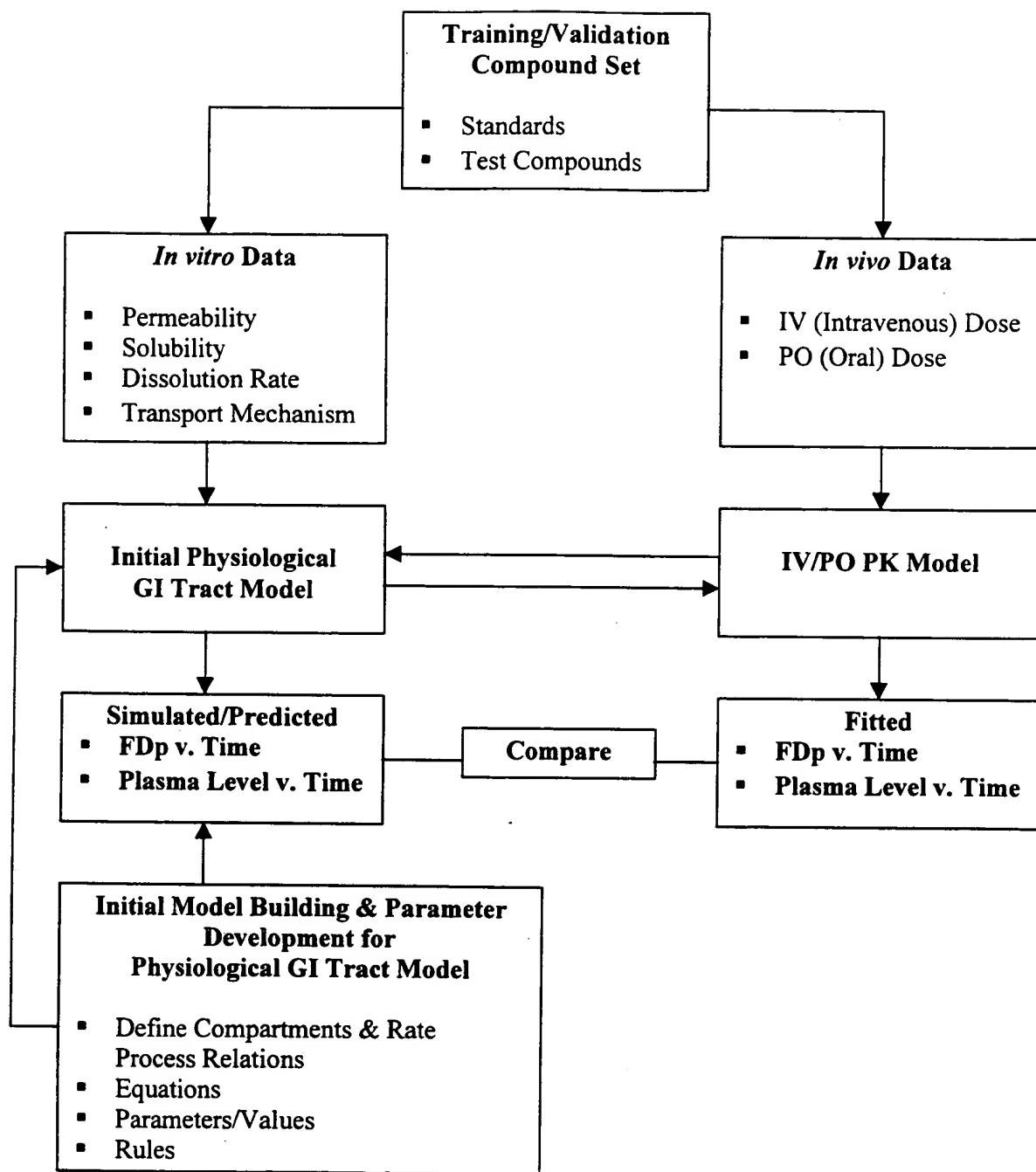


FIG. 20 "CE5850"

FIG. 21

Gastrointestinal Transit

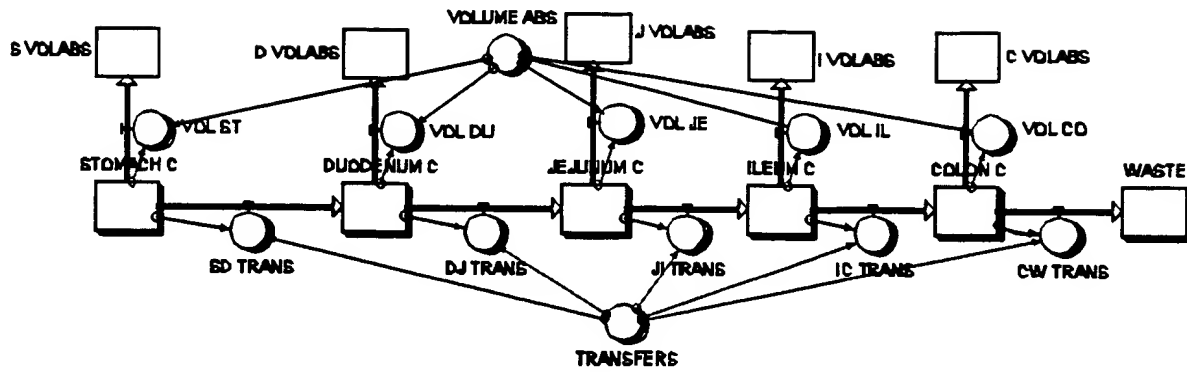


FIG. 22

pH Dependent Solubility and Dissolution

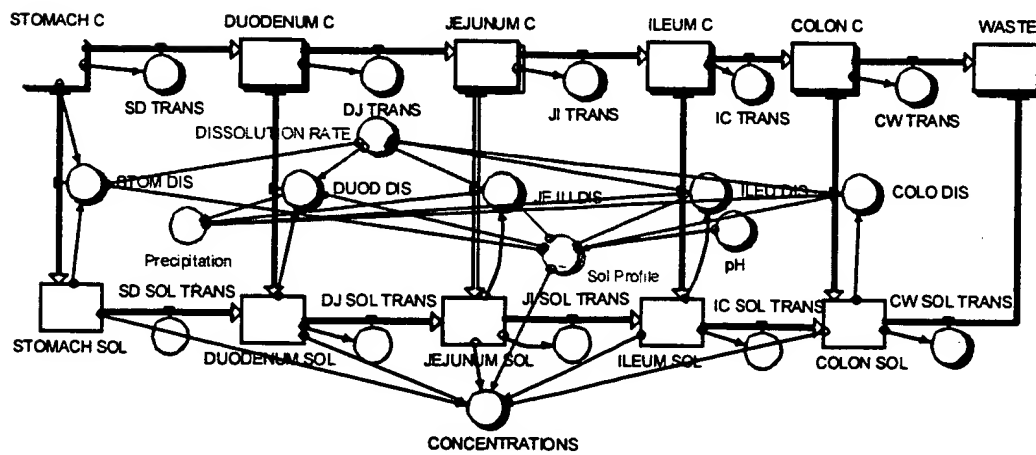


FIG. 23

Absorption

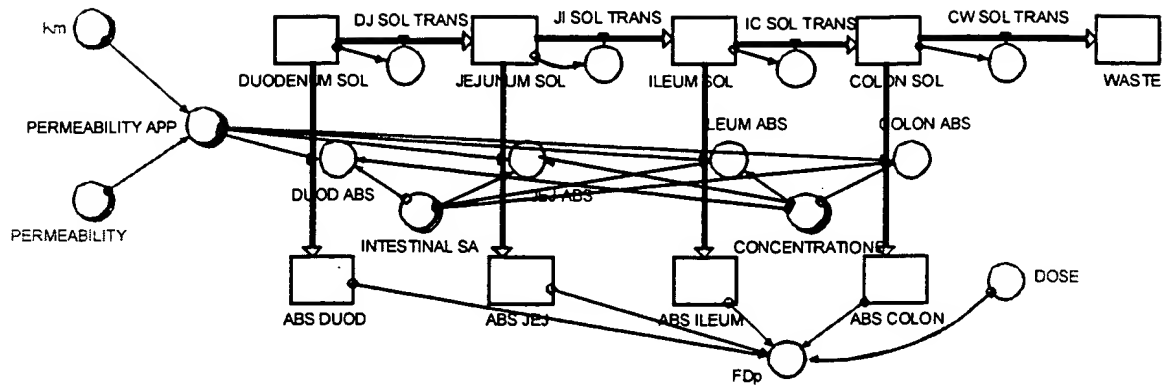


FIG. 24

GI Tract -Intestinal Model

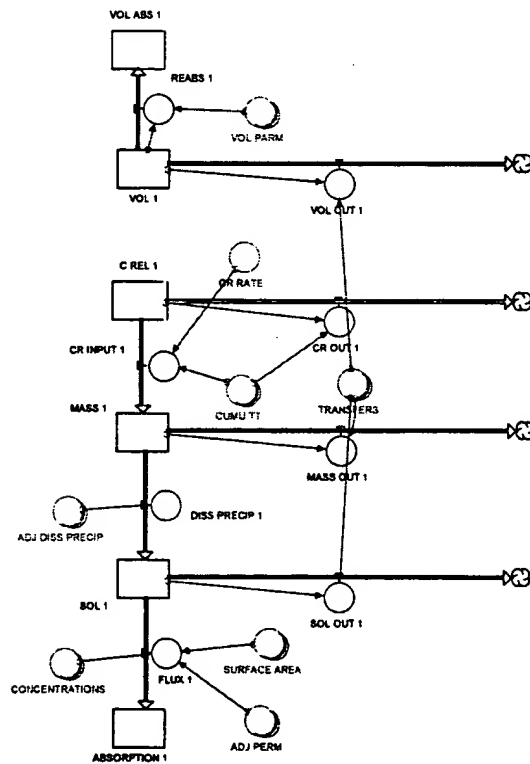
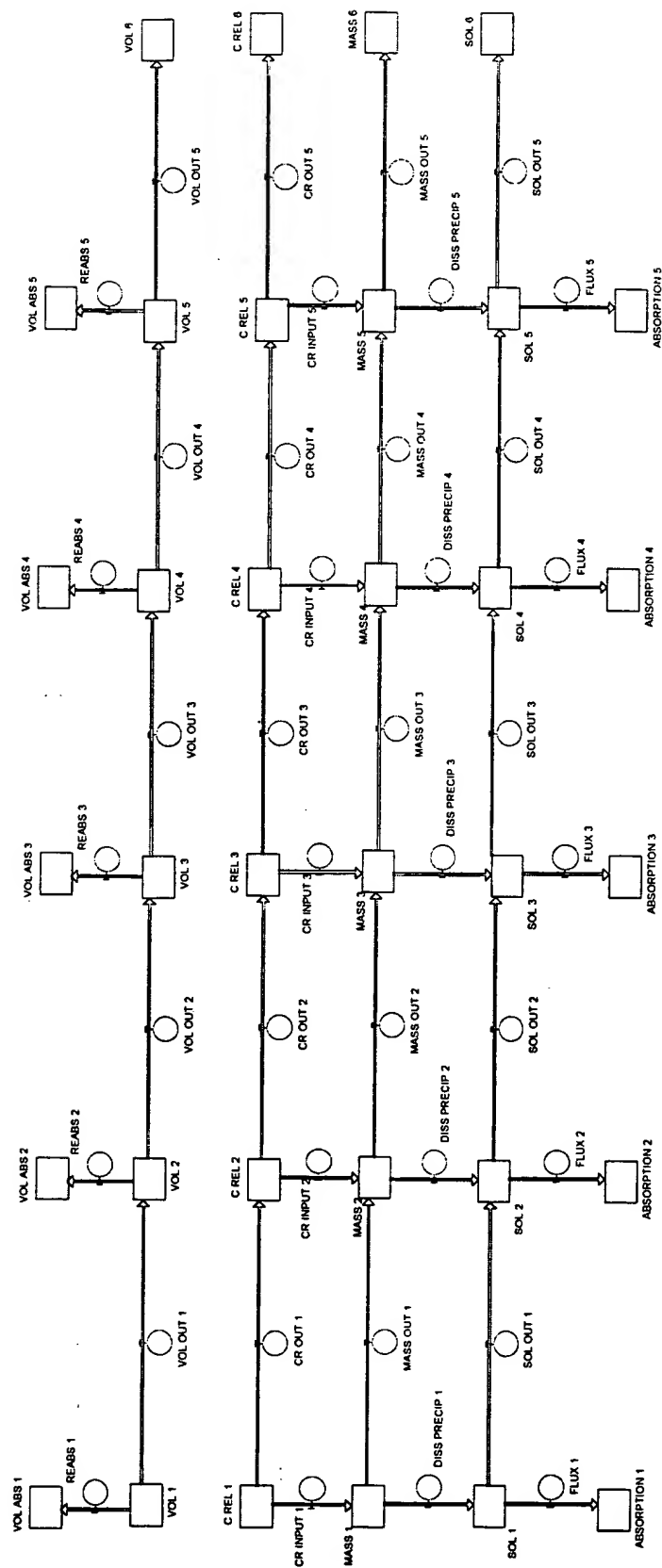


FIG. 25

GI Tract-Intestinal Model (without converters, ghosts or connectors)



GI Tract-Intestinal Model

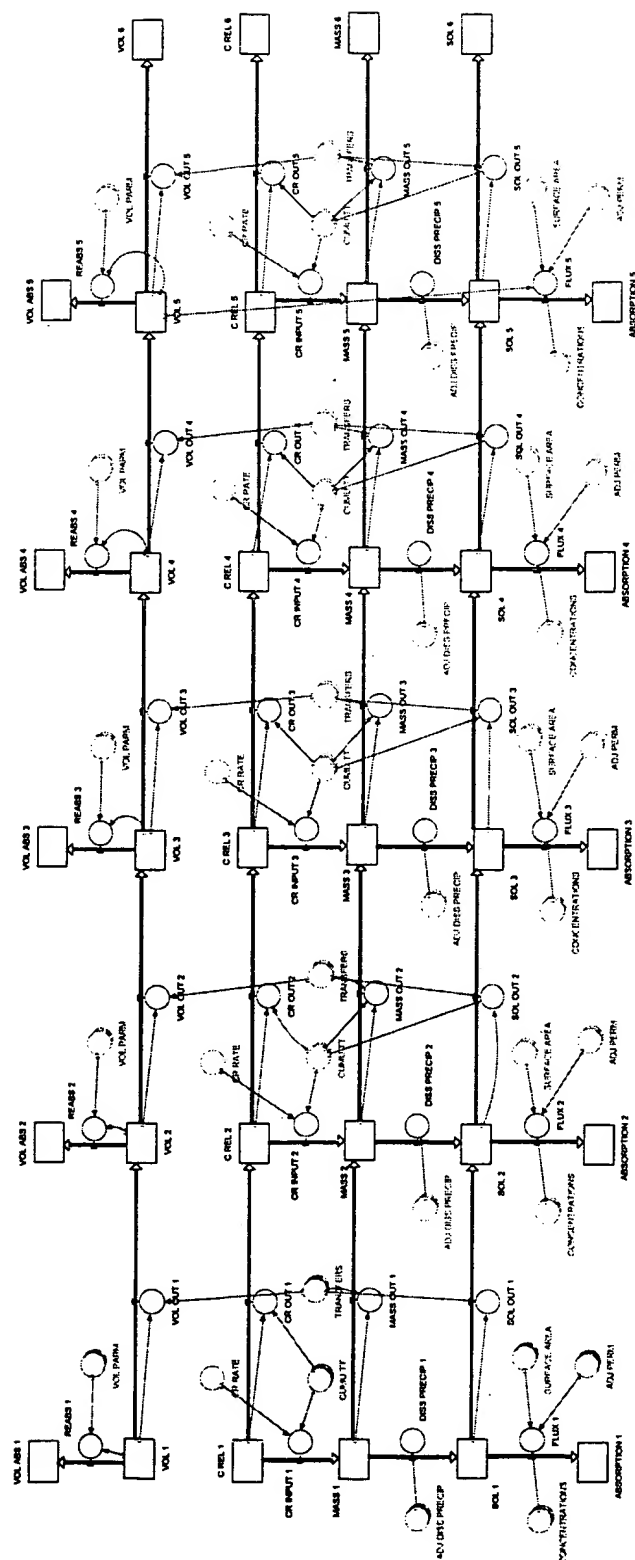


FIG. 27

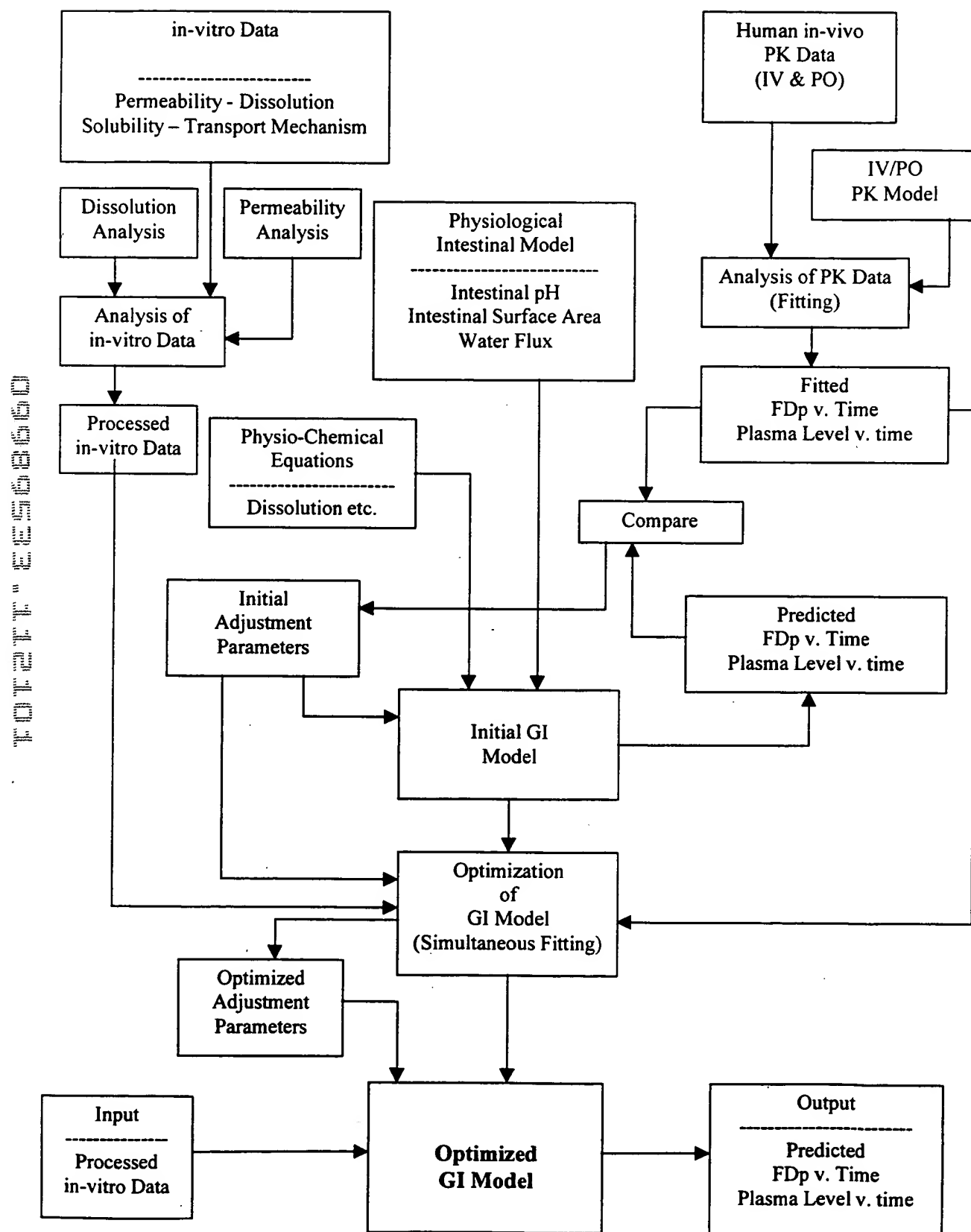


FIG. 28

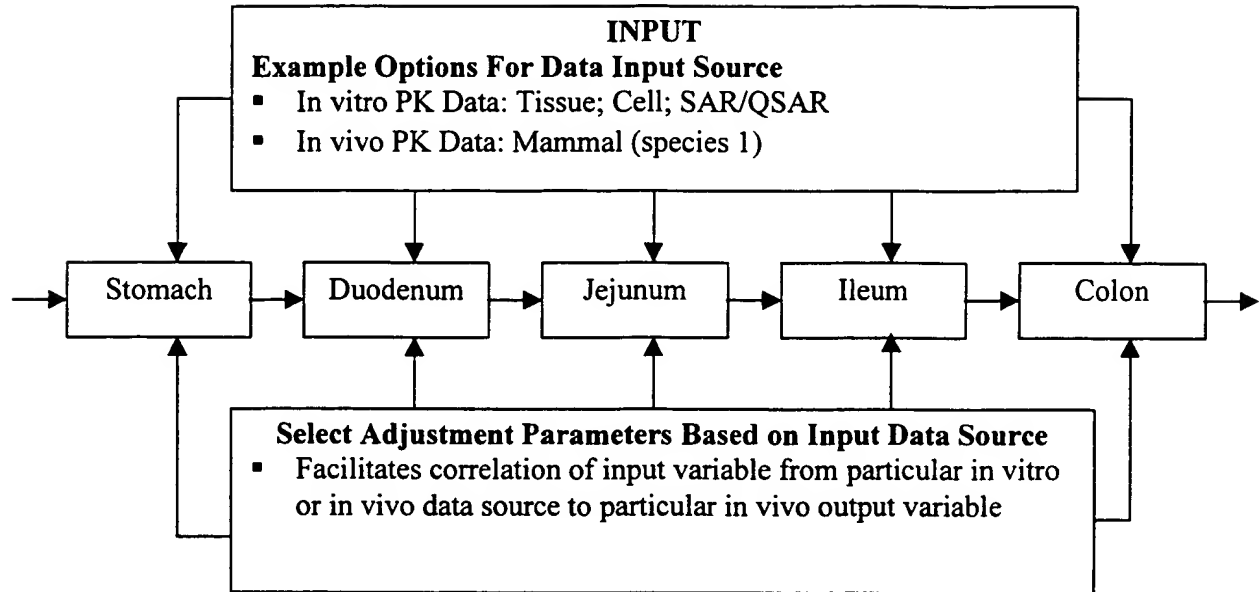


FIG. 29

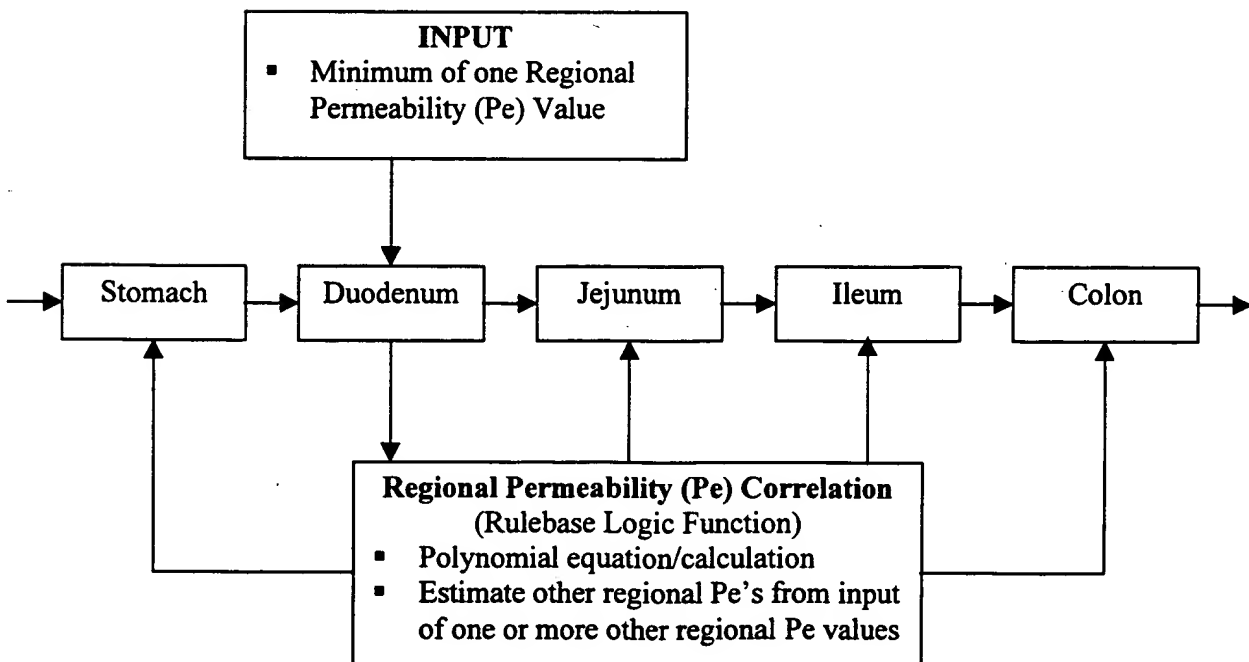


FIG. 30

Parameters

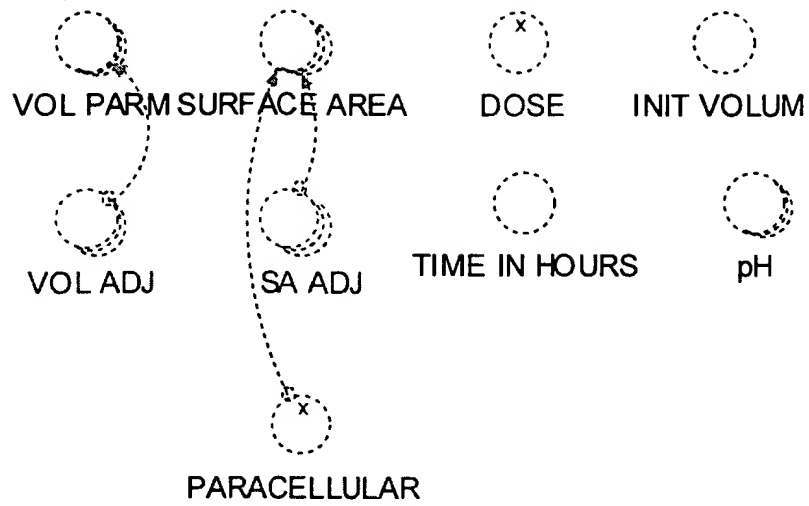


FIG. 31

Transit Time

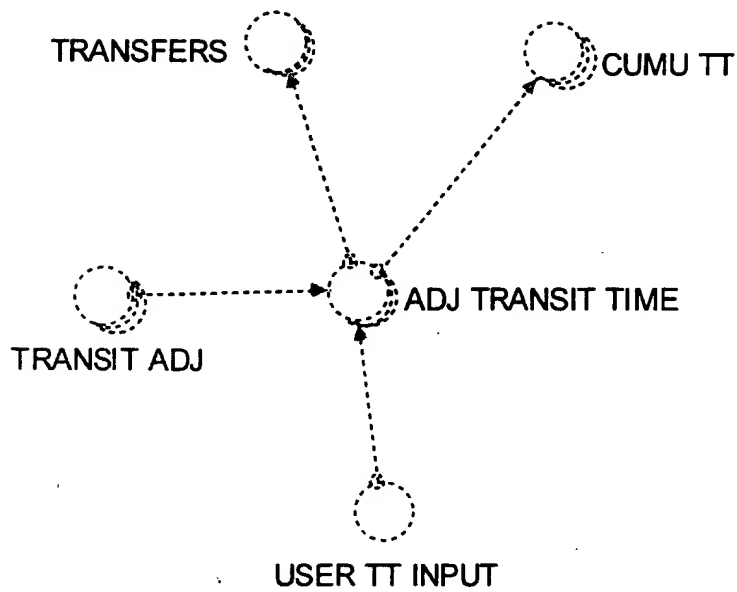


FIG. 32

Permeability Calculation

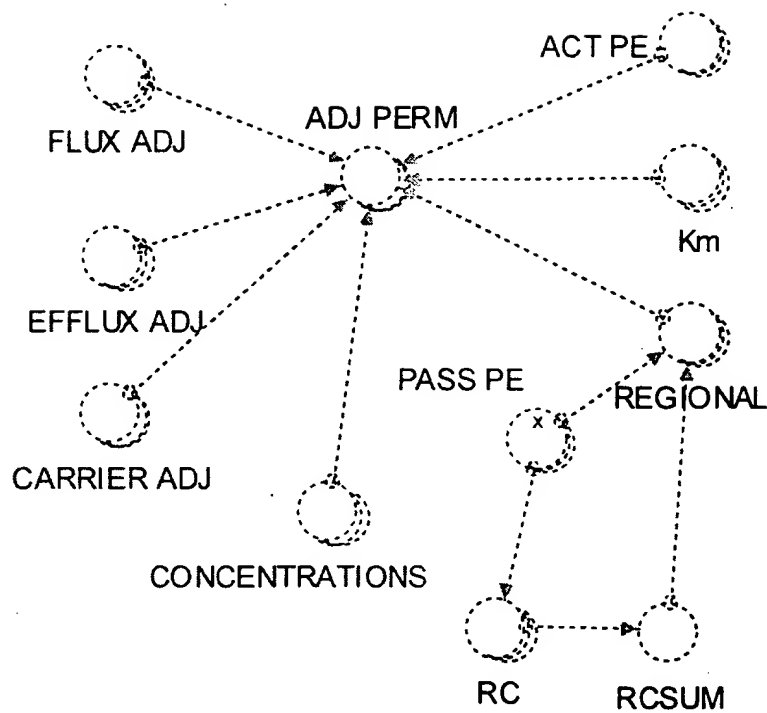


FIG. 33

Solubility Calculation

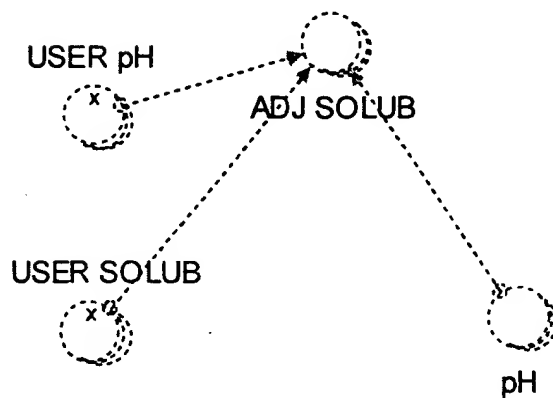


FIG. 32 "EE568660"

FIG. 34

Control Release Calculation

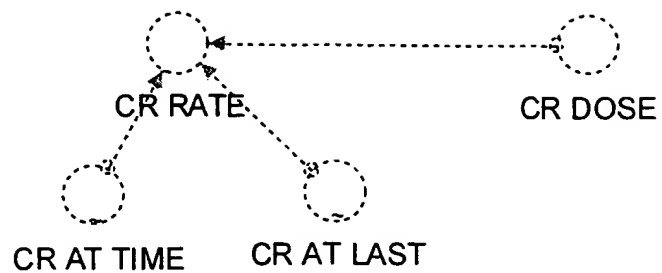


FIG. 35

Concentration Calculation

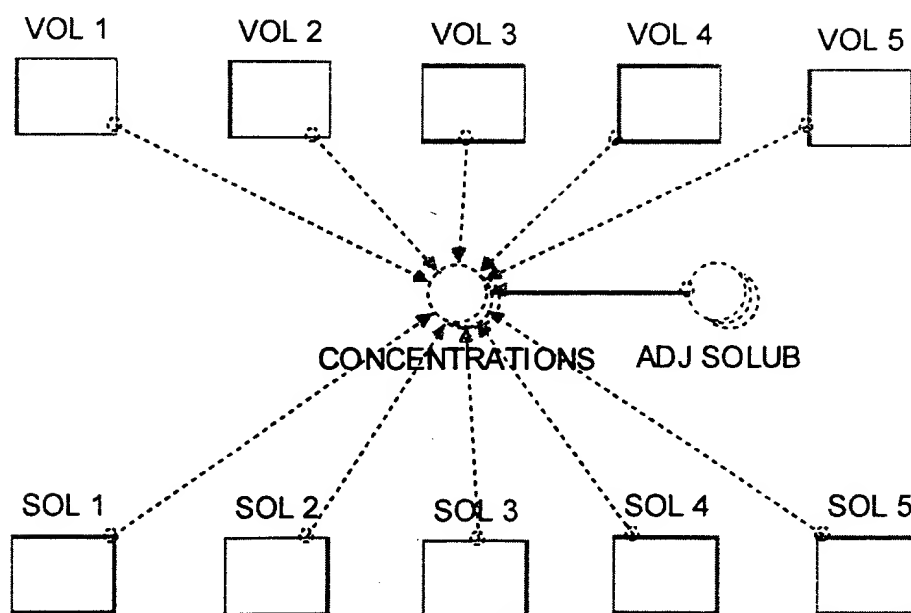


FIG. 34

FIG. 36

Dissolution Calculation

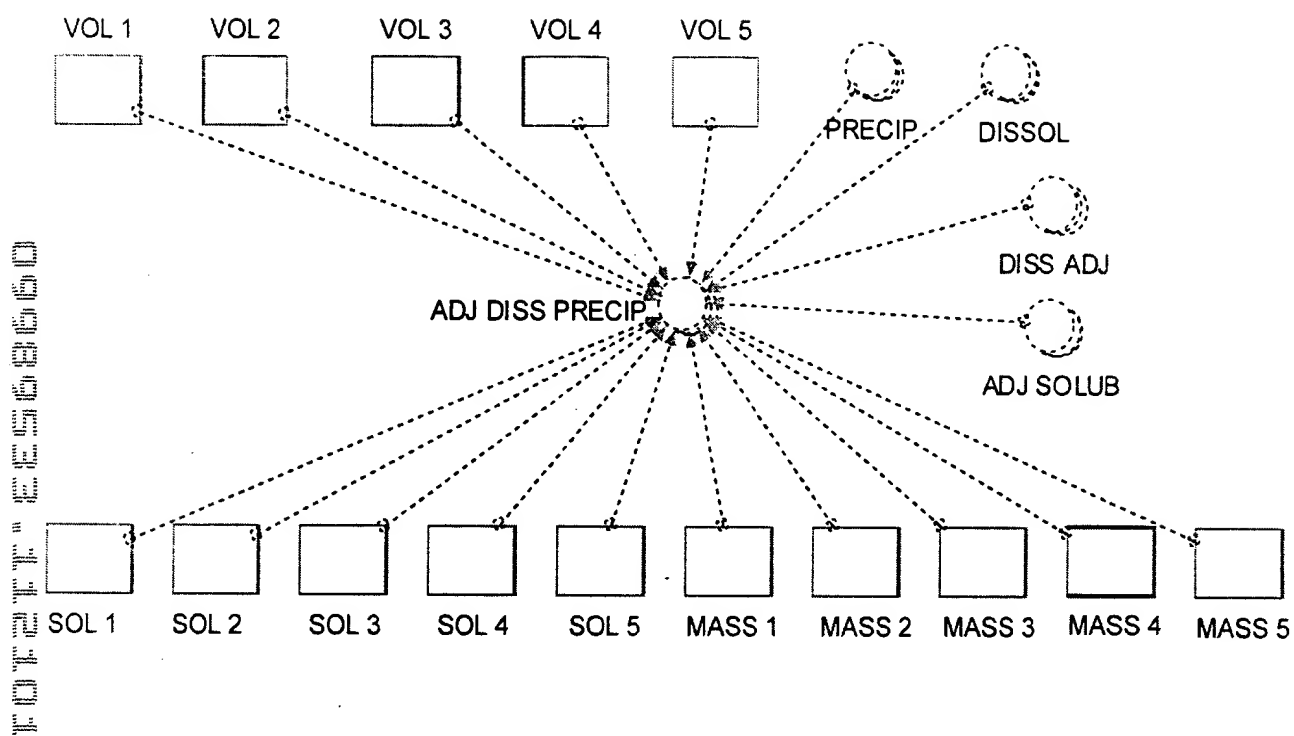


FIG. 37

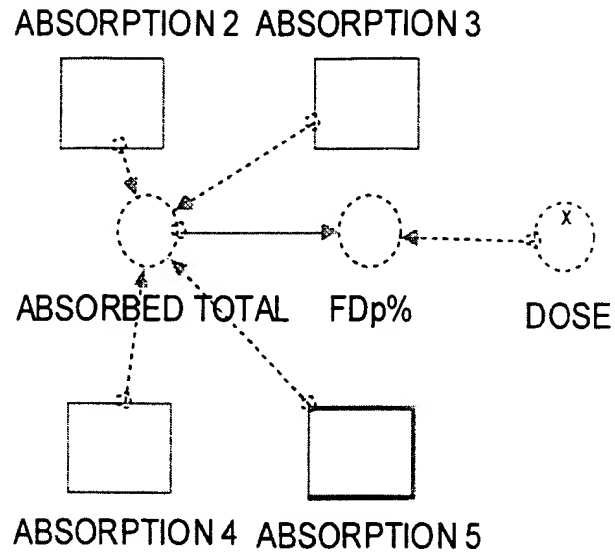


FIG. 38

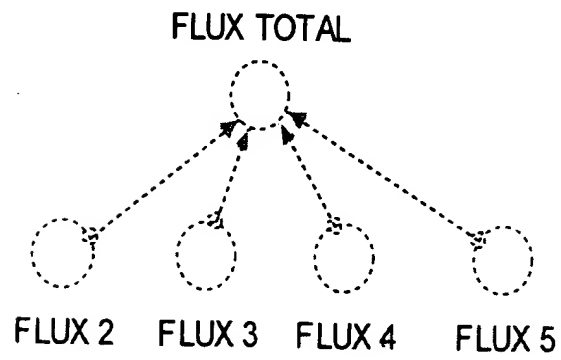


FIG. 39

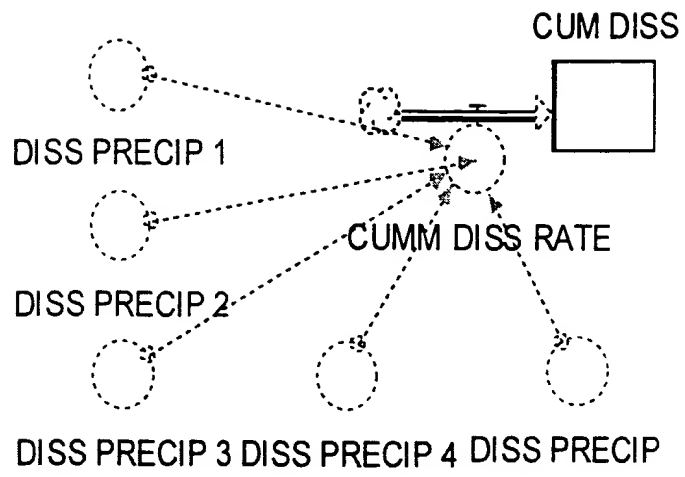


FIG. 40

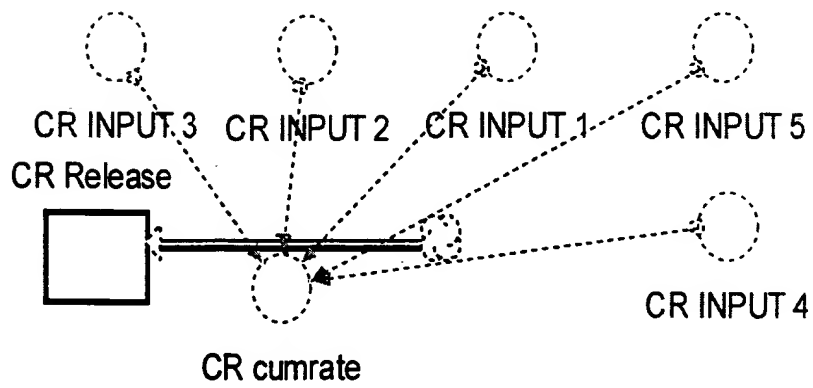


FIG. 39

FIG. 41

Physiological GI Tract Model

Database

- **GI Segment Compartments**
 - Fluid Absorption
 - Fluid Volume
 - Insoluble Mass
 - Soluble Mass
 - Soluble Mass Absorption
 - Dosage Form Mass
- **GI Segment Flow Regulators**
 - Fluid Absorption Rate
 - Fluid Volume Transit Rate
 - Insoluble Mass Transit Rate
 - Insoluble Mass Dissolution Rate
 - Soluble Mass Transit Rate
 - Soluble Mass Absorption Rate
 - Dosage Form Disintegration/Release Rate
- **GI Segment Converters**
 - Fluid Volume Absorption Rate Constant
 - GI Transit Rate Constant
 - Adjusted Dissolution Rate Constant
 - Dissolved Drug Concentration
 - Adjusted Surface Area
 - Adjusted Permeability

Rulebase

- GI Transit
- Dissolution
- Absorption
- Permeability Calculations
- Concentration Calculations
- Computational Error Corrections

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FIG. 42

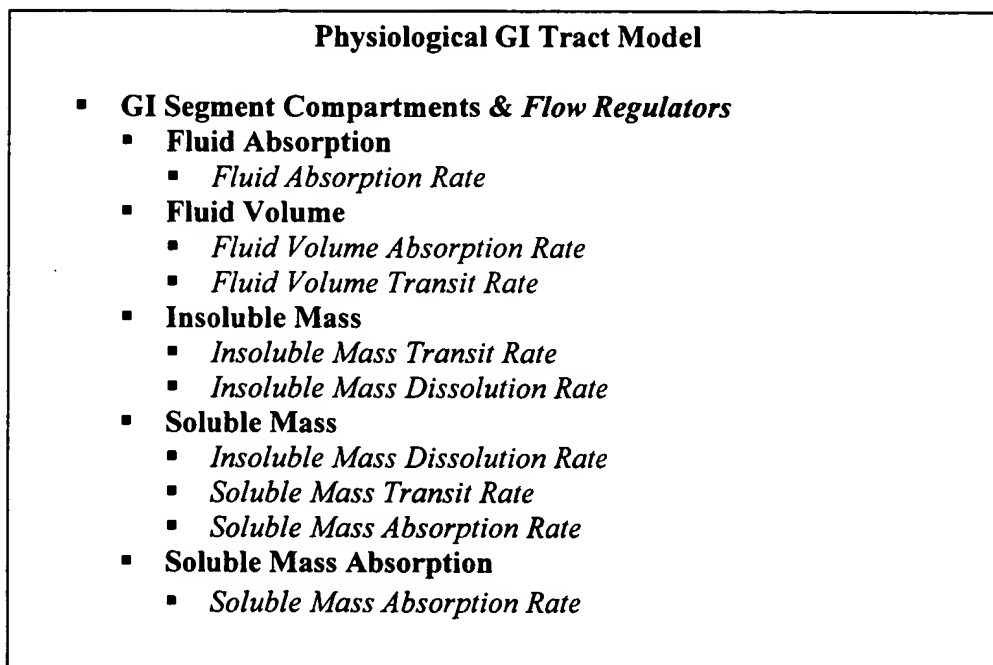


FIG. 43

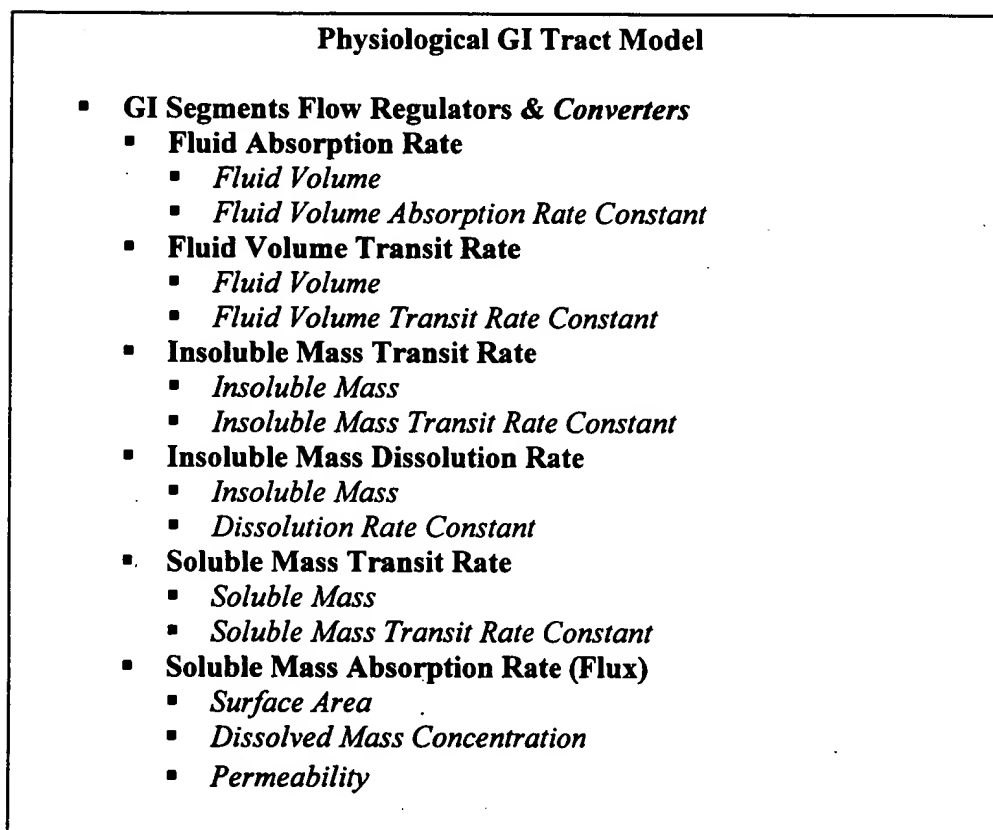


FIG. 44

Physiological GI Tract Model

- **Converters**
 - Permeability
 - Passive Absorption Adjustment Parameter
 - Efflux/Secretion Adjustment Parameter
 - Active Absorption Adjustment Parameter
 - Active or Carrier Mediated Absorptive Permeability
 - Km
 - Passive Permeability/Regional Correlation
 - Passive Permeability
 - Logic Function For Regional Correlation
 - Passive Permeability
 - Logic Function For Regional Correlation
 - Dissolved Mass Concentrations
 - Dissolved Mass Concentration
 - Fluid Volume
 - Solubility
 - pH
 - Solubility
 - Dissolution Rate Constant
 - Fluid Volume
 - Precipitation Rate Constant
 - Dissolution Rate Adjustment Parameter
 - Solubility
 - Insoluble Mass
 - Soluble Mass
 - Surface Area
 - Surface Area Adjustment Parameter
 - Transport Mechanism
 - Transit Rate
 - Transit Time Adjustment Parameter
 - User Adjusted Transit Time
 - Fluid Volume Absorption Rate Constant
 - Fluid Volume Adjustment Parameter

FIG. 45

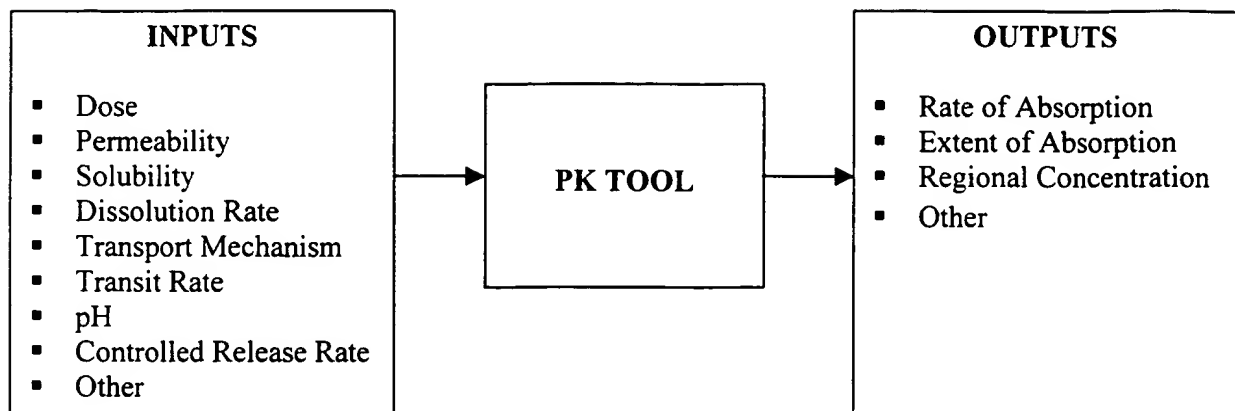


FIG. 46

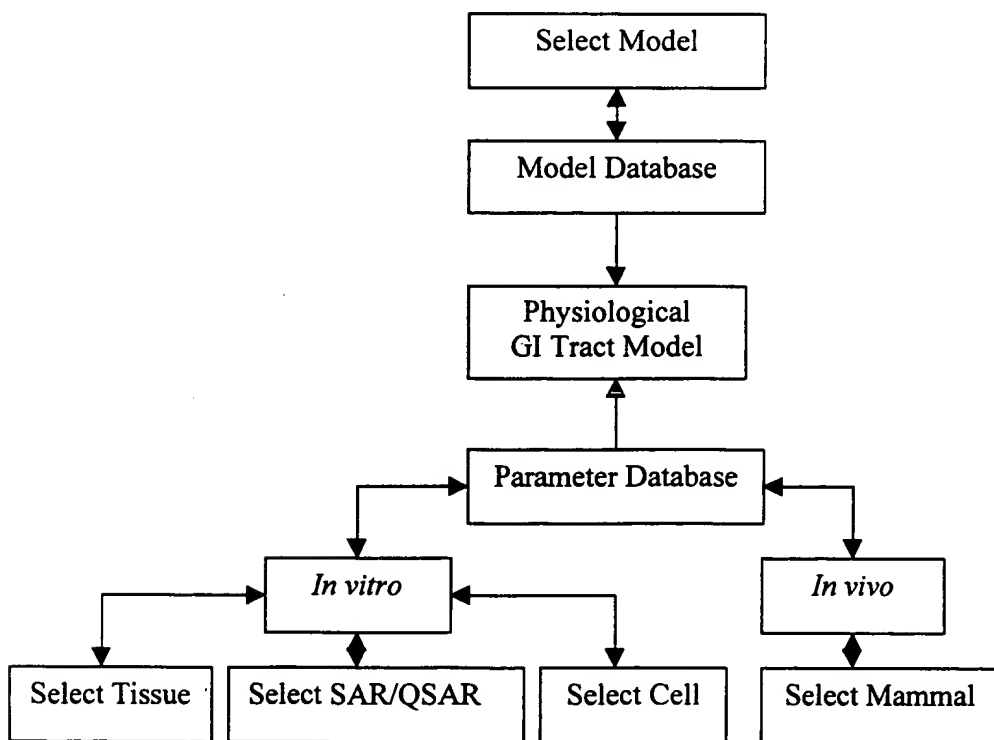


FIG. 47

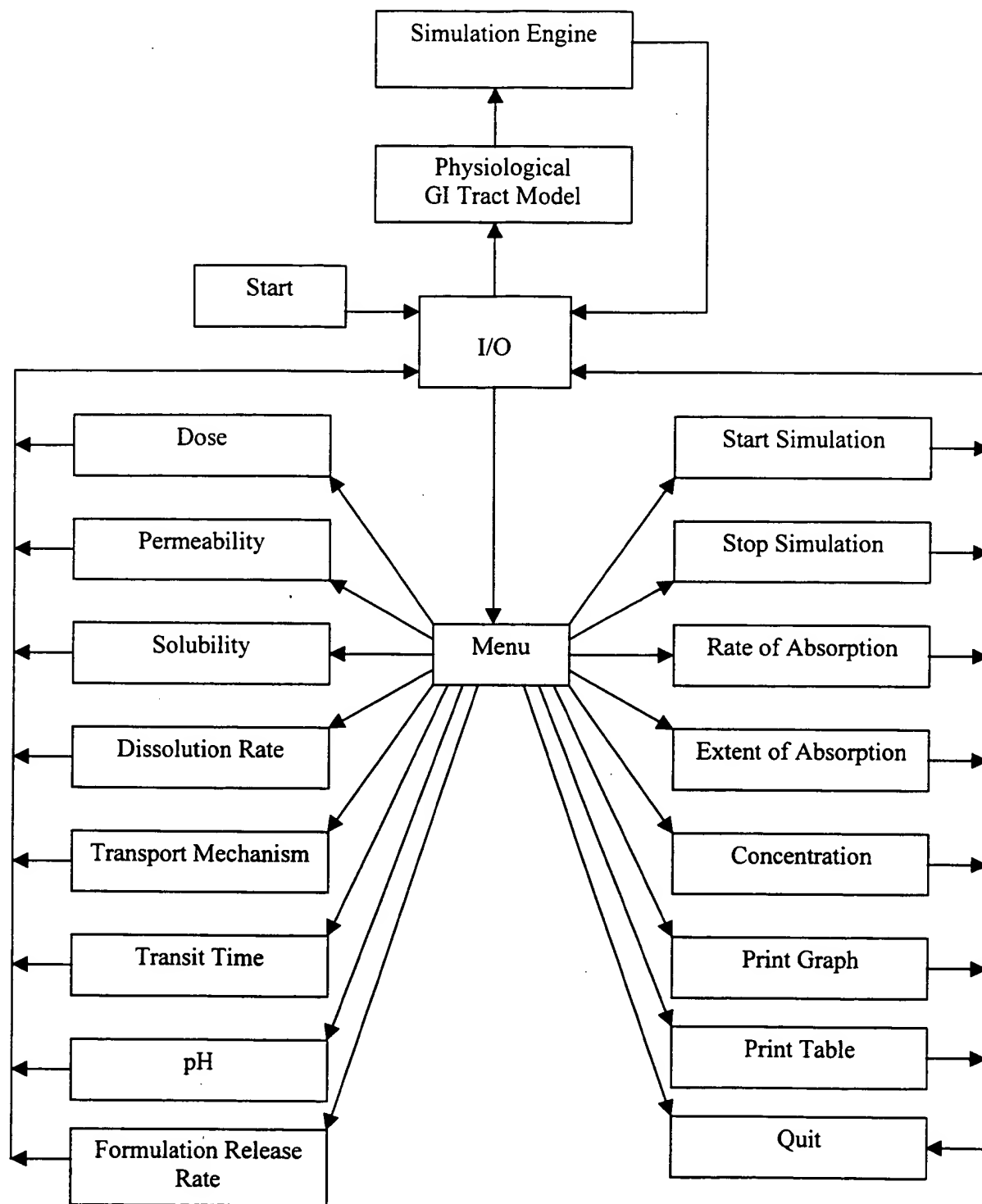


FIG. 47 "EE58550"

FIG. 48

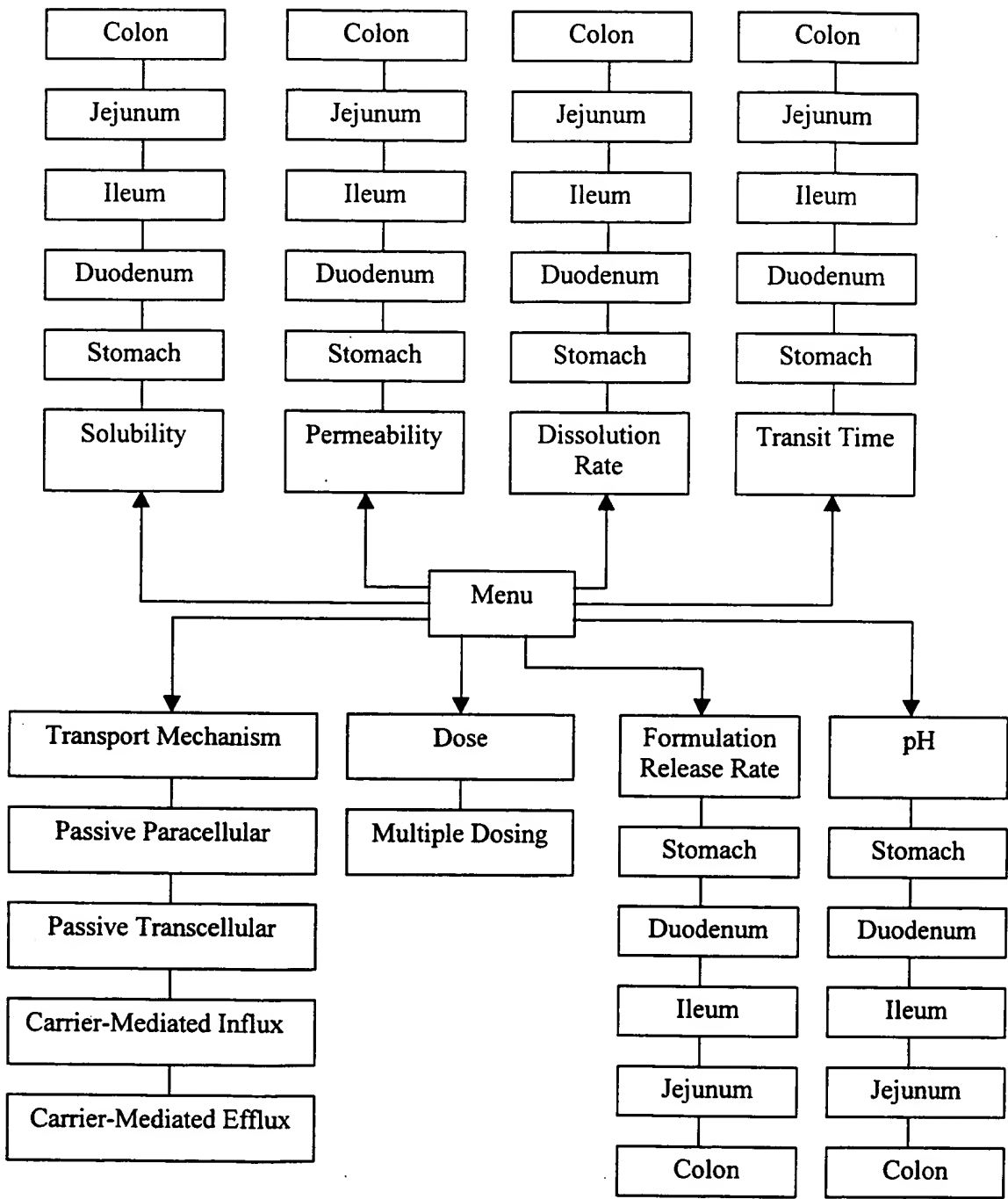


FIG. 48

FIG. 49

Correlation of FDp Extent - GI Model and Pharmacokinetic data

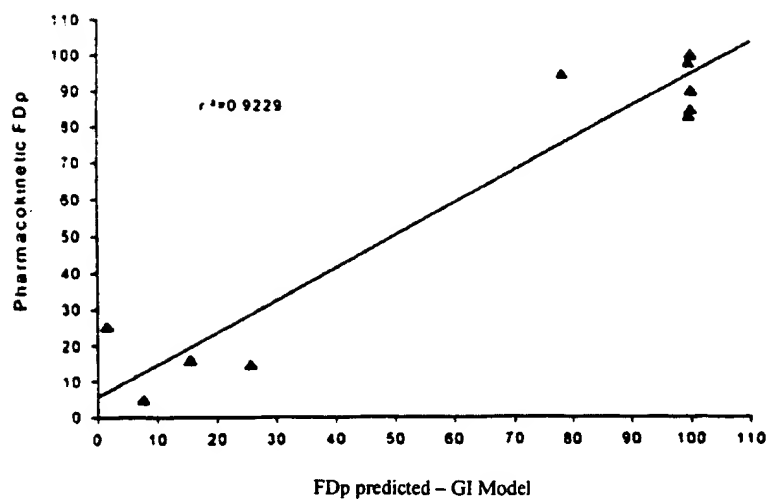


FIG. 50

Correlation of FDp rate of absorption - GI Model and Pharmacokinetic Data

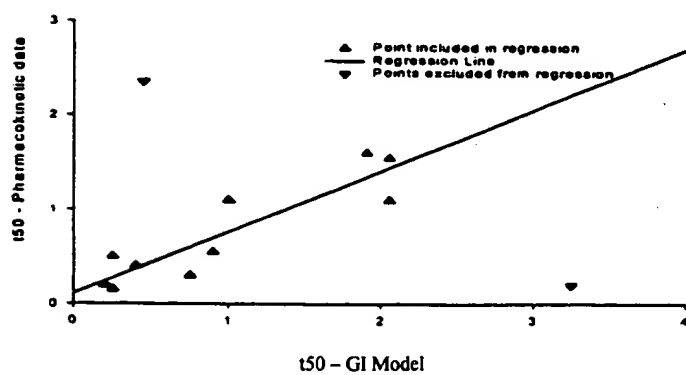


FIG. 51

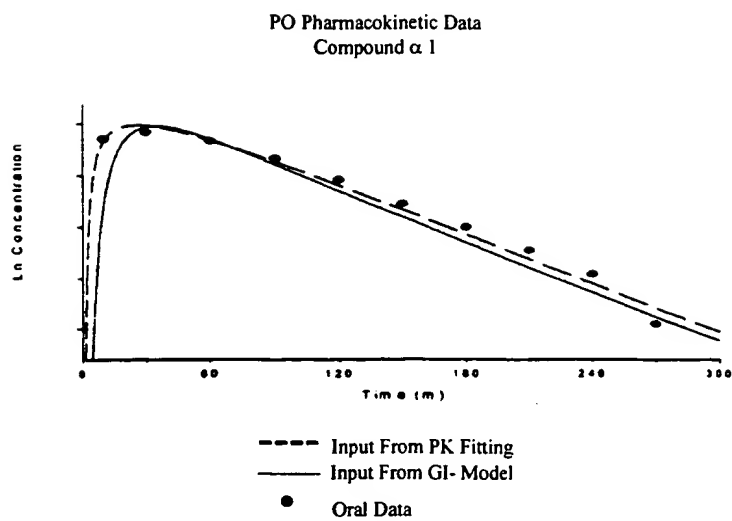


FIG. 52

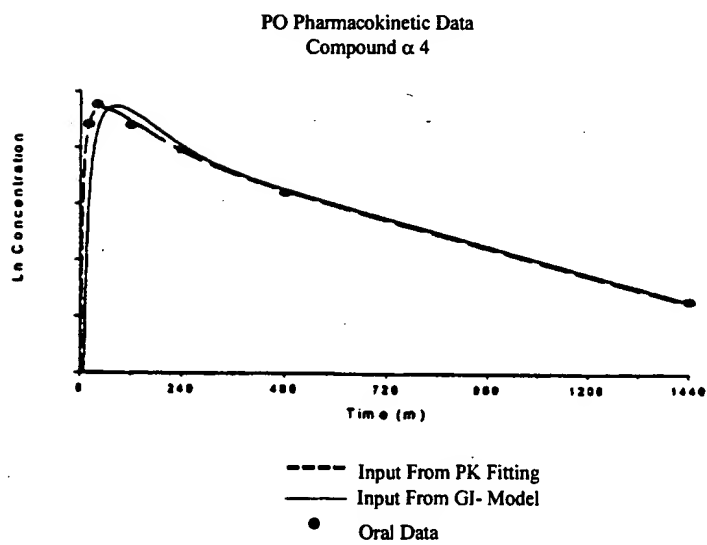
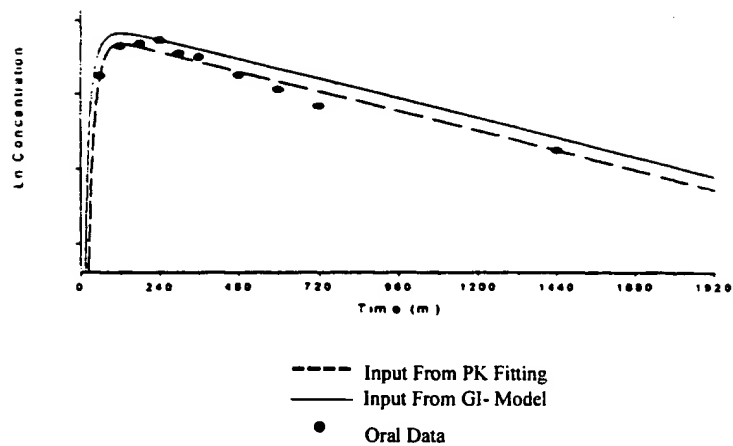


FIG. 53

PO Pharmacokinetic Data
Compound β 6



FOR "EES660"

FIG. 54

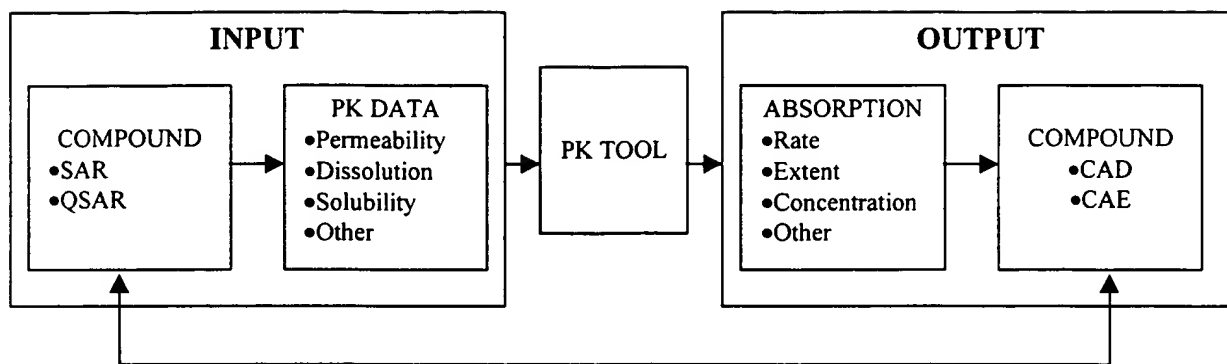


FIG. 55

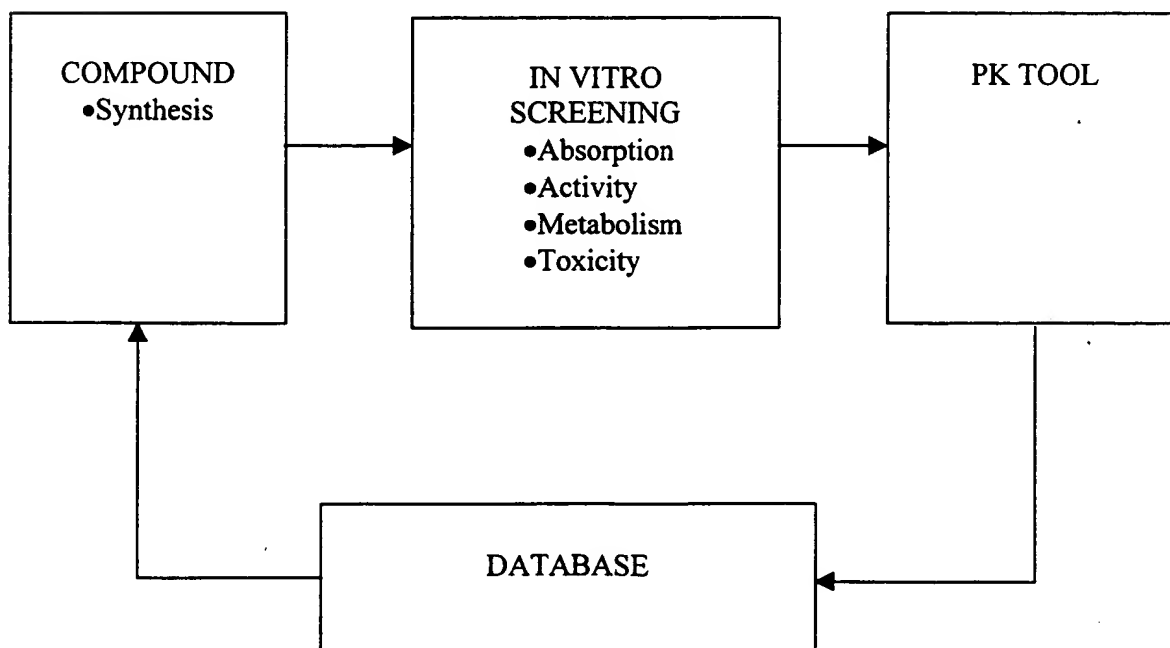


FIG. 54